May 6, 2020

DiaSorin Inc.
Mari Meyer
Vice President of Regulatory & Clinical Affairs
1951 Northwestern Ave
Stillwater, MN 55082-0285

Re: K192586
Trade/Device Name: Liaison® Folate
Regulation Number: 21 CFR 862.1295
Regulation Name: Folic Acid Test System
Regulatory Class: Class II
Product Code: CGN
Dated: May 1, 2020
Received: May 4, 2020

Dear Mari Meyer:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part

801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Marianela Perez-Torres, Ph.D.
Acting Deputy Director
Division of Chemistry
and Toxicology Devices
OHT7: Office of In Vitro Diagnostics
and Radiological Health
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*
K192586

Device Name
LIAISON® Folate

Indications for Use *(Describe)*
The DiaSorin LIAISON® Folate assay uses chemiluminescent immunoassay (CLIA) technology for the quantitative determination of Folic acid in human serum. Folic acid measurements are used in the diagnosis and treatment of anemias. Assay results should be used in conjunction with other clinical or laboratory data to assist the clinician in making individual patient management decisions.
The assay must be performed on the LIAISON® XL Analyzer.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

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510(k) Summary

LIAISON® Folate

This summary of 510(k) safety and effectiveness information is submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

1. 510(k) Number: K192586

2. Applicant:
Mari Meyer
Vice President of Regulatory and Clinical Affairs
DiaSorin Inc.
1951 Northwestern Avenue, P.O. Box 285**,** Stillwater, MN 55082-0285
Office Number: 651-351-9710; Fax Number: 651-351-5669
Email: mari.meyer@diasorin.com

3. Date: May 5, 2020

4. Proprietary and Established Names:

LIAISON® Folate

5. Regulatory Information:

Classification Name: Folic acid test system
Trade Name: LIAISON® Folate
Common Name: Folate
Regulation: 21 CFR 862.1295
Classification: Class II
Panel: Clinical Chemistry (75)
Product Code: CGN

6. Predicate Devices:
The predicate device used to demonstrate substantial equivalence to the LIAISON® Folate Assay is the Abbott Laboratories, ARCHITECT Folate, (K092740).

7. Device Description:
The LIAISON® Folate assay is a competitive chemiluminescence immunoassay (CLIA) for quantitative determination of Folic acid in serum. During the first incubation, Folic acid is dissociated from its binding protein. After five (5) minutes, a high pH buffer is added to prevent re-association to the binding protein. After five (5) minutes, Folic acid binds to a Folate Binding Protein on the solid phase, which competes with a Folic acid linked to an isoluminol derivative. After a third incubation, the unbound material is removed with a wash cycle. Subsequently, the starter reagents are added to initiate a flash chemiluminescent reaction. The light signal is measured by a photomultiplier as relative light units (RLU) and is inversely proportional to the concentration of Folic acid present in calibrators, controls, or samples.

8. Intended Use:
The DiaSorin LIAISON® Folate Assay uses chemiluminescent immunoassay (CLIA) technology for the quantitative determination of Folic acid in human serum. Folic acid measurements are used in the diagnosis and treatment of anemias. Assay results should be used in conjunction with other clinical or laboratory data to assist the clinician in making individual patient management decisions.

The assay must be performed on the LIAISON® XL Analyzer.

9. Indication(s) for Use:
Same as Intended Use

10. Substantial Equivalence Information:
A comparison of the similarities and differences between the LIAISON® Folate and the predicate is provided below:

Assay - Similarities and Differences		
Characteristic	**Candidate Device** **LIAISON® Folate**	**Predicate Device** **Abbott Laboratories, ARCHITECT Folate (K092740)**
Intended Use	The DiaSorin LIAISON® Folate assay uses chemiluminescent immunoassay (CLIA) technology for the quantitative determination of Folic acid in human serum. Folic acid measurements are used in the diagnosis and treatment of anemias. Assay results should be used in conjunction with other clinical or laboratory data to assist the clinician in making individual patient management decisions. The assay must be performed on the LIAISON® XL Analyzer.	The ARCHITECT Folate assay is a chemiluminescent microparticle Folate Binding Protein assay for the quantitative determination of folate in human serum and plasma on the ARCHITECT iSystem. Folate measurements are used in the diagnosis and treatment of megaloblastic anemia.
Measured Analyte	Folate	Same
Assay Type	Chemiluminescence Immunoassay	Same
Results	Quantitative	Same
Sample Type	Human Serum	Human Serum & Plasma
Sample size	50 µL	150 µL
Storage	2-8°C	Same
Operating Principle	Automated Chemiluminescence Immunoassay (CLIA)	Same
Solid Phase	Magnetic particles coated with bovine folate binding protein	Microparticles coated with mouse monoclonal antibodies bound to bovine folate binding protein

Assay - Similarities and Differences		
Characteristic	**Candidate Device** **LIAISON® Folate**	**Predicate Device** **Abbott Laboratories, ARCHITECT Folate (K092740)**
Conjugate	Folic acid conjugated to an isoluminol derivative	Acridinium labeled pteroic acid
Analytical Measuring Range	1.6 ng/mL - 20 ng/mL	Same

11. Standard/guidance Document Reference:

- CLSI Guideline EP5-A3, Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline.
- CLSI Guideline EP15-A3, User Verification of Precision and Estimation of Bias; Approved Guideline.
- CLSI Guideline EP07-A2, Interference Testing in Clinical Chemistry, Approved Guideline.
- CLSI Guideline EP06-A, Evaluation of the Linearity of Quantitative Measurement Procedures; A Statistical Approach; Approved Guideline.
- CLSI Guideline EP 17-A2, Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline.
- CLSI EP37-A: Supplemental Tables for Interference Testing in Clinical Chemistry; First Edition, April 2018.
- CLSI Guideline EP09-A3, Measurement Procedure Comparison and Bias Estimation Using Patient Samples; Approved Guideline.
- CLSI Guideline EP28-A3C, Defining, Establishing and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline.

12. Performance Characteristics:

Method Comparison

A total of 157 human serum samples spanning the assay range, were tested by the LIAISON® Folate and by another commercially available method following CLSI EP9-A3. The study yielded the following Passing & Bablok regression analysis: LIAISON® Folate = (y = 0.96x - 0.61); R = 0.948

Bias at the medical decision level:

Medical Decision level	Bias	95% confidence interval
4.41 ng/mL	-0.772 ng/mL	-1.550 to -0.130 ng/mL

Expected Values

It is recommended that each laboratory establish its own range of expected values for the population taken into consideration.

To assess the expected reference range for the LIAISON® Folate assay, a study was performed with prospectively collected serum samples from 166 apparently healthy

adults 21 - 59 years of age from mixed ethnic backgrounds (30% Caucasian, 32% African Americans and 38% Hispanics) who were fasting for at least eight (8) hrs. Apparently healthy status was determined by subjects who had no history of anemias, Folic acid or B12 deficiency, IBD or suspected IBD, celiac disease, gastrointestinal malabsorption disorders, or eating disorders. No oral contraceptive use within three (3) months and no alcohol within 48 hours of blood draw. No pregnant women or anyone taking folic acid supplementation were included in the study population.
Based on the 95% Confidence Interval the following values were established according to CLSI guideline C28-A3.

	Observed Reference Ranges	
Population (n=166)	Median	Observed Range 2.5^{th} to 97.5^{th} Percentile
United States	8.22 (ng/mL)	3.96 ng/mL – 16.70 (ng/mL)

Precision

Two (2) kit controls and six (6) samples containing concentrations of analyte prepared to span the range of the assay were assayed twice per day in duplicate, over 20 operating days using two (2) reagent lots, to determine repeatability and reproducibility of the LIAISON® Folate assay.

Results Table for Combined Lots

Sample ID	n	mean (ng/mL)	Repeatability (Between-Lot)		Reproducibility (Total Across Lots)	
			SD	%CV	SD	%CV
Kit Control 1	160	4.79	0.14	2.9%	0.25	5.3%
Kit Control 2	160	12.33	0.23	1.8%	0.52	4.3%
Precision Serum 1	160	2.90	0.18	6.4%	0.20	7.0%
Precision Serum 2	160	4.57	0.18	3.9%	0.27	5.8%
Precision Serum 3	160	7.87	0.14	1.8%	0.40	5.1%
Precision Serum 4	160	10.2	0.04	0.4%	0.50	4.9%
Precision Serum 5	160	12.1	0.08	0.7%	0.64	5.3%
Precision Serum 6	160	14.1	0.22	1.6%	0.72	5.1%

Results Table for Single Lot

Sample ID	n	mean (ng/mL)	Within-Run		Run-to-Run		Day-to-Day		TOTAL (Within-lot)	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV
Control 1	80	4.69	0.22	4.7%	0.05	1.0%	0.13	2.9%	0.26	5.6%
Control 2	80	12.49	0.29	2.3%	0.29	2.3%	0.40	3.2%	0.57	4.6%
Serum 1	80	2.77	0.11	4.1%	0.14	5.2%	0.10	3.7%	0.21	7.6%
Serum 2	80	4.44	0.13	3.0%	0.21	4.7%	0.10	2.3%	0.27	6.0%
Serum 3	80	7.77	0.20	2.6%	0.20	2.5%	0.35	4.5%	0.45	5.8%
Serum 4	80	10.24	0.26	2.5%	0.16	1.6%	0.50	4.9%	0.58	5.7%
Serum 5	80	12.10	0.30	2.5%	0.46	3.8%	0.53	4.4%	0.76	6.3%
Serum 6	80	14.24	0.33	2.3%	0.32	2.2%	0.73	5.1%	0.84	6.1%

Linearity

One neat high serum sample containing endogenous Folate, above the measuring range of the assay at 20 ng/mL, was diluted with a contrived low serum sample for preparing the dilution series. The dilution series was analyzed by the LIAISON® Folate assay following CLSI EP6-A. The results were analyzed by regression of observed concentration versus expected concentration.

The resulting equation is:
Serum: Observed Folate = 1.011 (Expected) – 0.147; R = 0.999

Recovery

Seven (7) neat high concentration serum samples were analyzed with the LIAISON Folate assay. Recovery samples were then prepared by diluting the samples with the LIAISON Endocrinology Diluent according to the IFU. The results are provided in the following table.

Sample	Neat (ng/mL)	Calculated dilution 1:3 (ng/mL)	Diluted 1:3 (ng/mL)	% recovery
S1	22.9	5.73	5.83	101.8%
S2	30.6	7.65	7.71	100.8%
S3	*18.5	4.63	4.95	107.0%
S4	*19.6	4.90	4.86	99.2%
S5	38.4	9.60	10.6	110.4%
S6	27.9	6.98	6.81	97.6%
S7	23.4	5.85	5.87	100.3%

Analytical Specificity

Cross-Reactivity

Controlled Studies of potentially cross-reacting substances were performed on the LIAISON® Folate assay at the concentrations listed below. The testing was based on CLSI-EP7-A2.

Cross-Reactant	**Spiked Concentration**	**% Cross Reactivity**
Aminopterin	490 ng/mL	0.488%
Phenytoin	201,400 ng/mL	0.000%
Methotrexate (Amethopterin)	1,000 ng/mL	0.781%%
Folinic Acid (Leucovorin)	500 ng/mL	1.730%

Interfering Substances

Controlled studies of potentially interfering substances performed serum at 2 levels showed no interference in the LIAISON® Folate at the highest concentration for each substance listed below. The testing was based on CLSI-EP7-A2.

Drug/Substance	**Concentration Tested**

Hemoglobin	30 mg/dL
Bilirubin (conjugated)	35 mg/dL
Bilirubin (unconjugated)	40 mg/dL
Triglycerides	3,000 mg/dL
Cholesterol	500 mg/dL
Albumin	9 g/dL
Human IgG	7.5 g/dL
HAMA	807 ng/mL
Rheumatoid Factor	1000 IU/mL
Acetaminophen	20 mg/dL
Acetylsalicylic Acid	65 mg/dL
Ibuprofen	50 mg/dL
Biotin	2.5 mg/mL
Acetylcysteine	283 mg/dL
Ampicillin Na	1000 mg/dL
, Cefoxitin	660 mg/dL
Cyclosporin	5 mg/dL
Doxycycline hyclate	6.25 mg/dL
Levodopa	20 mg/dL
Methyldopa	20 mg/dL
Metronidazole	25 mg/dL
Phenylbutazone	40 mg/dL
Rifampicin	7.5 mg/dL
Theophylline	5 mg/dL
Ascorbic Acid	44 mg/dL

Limit of Blank, Limit of Detection and Limit of Quantitation

The Limit of Blank, Limit of Detection and Limit of Quantitation were determined according to CLSI EP17-A2: Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline June 2012- Second Edition.

The following limits were determined with the LIAISON® Folate assay:
The limits are reported in the following table:

LoB	LoD	LoQ
≤1.2 ng/mL	1.4 ng/mL	1.6 ng/mL

Stability

Product	Storage Conditions		Claimed stability
Reagent Integral	Open vial	2-8°C	6 weeks
Calibration curve	N/A	N/A	21 days

Traceability

The LIAISON® Folate Calibrators are traceable to the WHO IS 03/178 (pg/mL).

13. Conclusion:

The LIAISON® Folate assay is substantially equivalent in principle and performance to the Abbott Laboratories, ARCHITECT Folate.